

**This Page Is Inserted by IFW Operations  
and is not a part of the Official Record**

## **BEST AVAILABLE IMAGES**

**Defective images within this document are accurate representations of  
the original documents submitted by the applicant.**

**Defects in the images may include (but are not limited to):**

- **BLACK BORDERS**
- **TEXT CUT OFF AT TOP, BOTTOM OR SIDES**
- **FADED TEXT**
- **ILLEGIBLE TEXT**
- **SKEWED/SLANTED IMAGES**
- **COLORED PHOTOS**
- **BLACK OR VERY BLACK AND WHITE DARK PHOTOS**
- **GRAY SCALE DOCUMENTS**

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

**THIS PAGE BLANK (USPTO)**

## PATENT SPECIFICATION



NO DRAWINGS

948.714

Date of Application and filing Complete Specification: July 19, 1962.

No. 27874/62.

Application made in United States of America (No. 125,094) on July 19, 1961.

Complete Specification Published: Feb. 5, 1964.

© Crown Copyright 1964.

Index at acceptance:—C2, J12; C2, C(3A7V3A2, 3A7V3E1, 3A7V3H, 3A7V3J2, 3A7V3L, 3A10A4E, 3A10A5C, 3A10A5H, 3A10A5K, 3A10E3A1, 3A10E5F1A, 3A10E5F2A, 3A10E5F3A, 3A10E5H, 3A13A1A1, 3A13A1A2, 3A13A1D, 3A13A1F3, 3A13A1K, 3A13C6A, 3A13C10G, 3A13C10H).

International Classification:—C 07 c.

## COMPLETE SPECIFICATION

## Preparation and use of Grignard Reagents

We, GENERAL ELECTRIC COMPANY, a corporation organised and existing under the Laws of the State of New York, United States of America, residing at 1, River Road, Schenectady 5, New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention is concerned with a process for making Grignard reagents useful in the preparation of other chemical compounds. More particularly the invention relates to a process which comprises reacting in a Grignard solvent medium an olefinic compound

having the formula  $R-C=CH_2$  with an alkyl Grignard reagent having the formula  $R^1MgX$  in the presence of a catalyst selected from halides of titanium, halides of zirconium, alkoxides and aryloxides of titanium (also known as alkyl and aryl titanates), and alkoxides and aryloxides of zirconium (also known as aryl and alkyl zirconates), where R is a monovalent organic radical free of substituents reactive with compounds of the formula  $R^1MgX$ ,  $R^1$  is an alkyl radical of at least 2 carbon atoms (e.g., from 2 to 6, or more carbon atoms) having a hydrogen on the beta carbon atom, and X is a halogen (e.g., chlorine, bromine or iodine), thereby effecting an exchange between the olefinic compound and the Grignard reagent to produce a new reagent derived from the olefinic compound displaying reactions of a compound having the formula  $RC_2H_3MgX$  where R, and X have the above meanings. R may be either on the carbon adjacent to the Mg or on the carbon once removed from the Mg, e.g., as shown by the formulae  $RCH_2CH_2MgX$  and

[Price 4s. 6d.]

$$RCH-MgX.$$

$$CH_3$$

Grignard reagents are commonly prepared by reacting an organic halide, for instance, ethyl bromide, propyl bromide or phenyl bromide, with magnesium, usually in a solvent medium such as diethyl ether or tetrahydrofuran. The Grignard reagents thus obtained are among the most generally useful reagents in organic chemistry. They react with a wide variety of compounds, such as aldehydes, ketones, carbon dioxide, esters, orthoformates, cyanogen halides, oxiranes and chlorosilanes, to form alcohols, acetals and nitriles, within the framework of the usual Grignard reactions such as may be found in the book "Grignard Reactions of Nonmetallic Substances" by Kharasch and Reinmuth, published by Prentice-Hall (1954). The Grignard reagents prepared by the method of this invention undergo all of the reactions of Grignard reagents prepared in the conventional manner, and thus provide a means for preparing compounds (alcohols, acids and aldehydes) containing the  $RC_2H_3$ -group, where R has the meaning given above.

A limitation on the use of Grignard reagents in the past has been that the necessary organic halides used to make these reagents have not always been readily available. In addition, it is sometimes difficult to prepare the Grignard reagent directly by reaction of the organic halide with magnesium, even when the organic halide is available. It would, therefore, be highly desirable to be able to employ readily available and inexpensive alkyl halides such as ethyl bromide or propyl bromide, which readily form Grignard reagents and be able to react these Grignard reagents with readily available and inexpen-

sive olefins to produce new Grignard reagents which cannot easily be obtained by presently known methods.

5 It is therefore one of the objects of this invention to readily prepare Grignard reagents.

It is another object of the invention to prepare Grignard reagents from readily available starting materials.

10 It is a still further object of the invention to prepare Grignard reagents in which the organic part of the Grignard reagent is derived from readily available compounds which cannot be found available as a halide as readily or as inexpensively.

15 Other objects of the invention will become more apparent from the discussion which follows.

20 In accordance with our invention, we have discovered a flexible process for making Grignard reagents from readily available starting materials to prepare in good yields and with a minimum of control problems Grignard reagents of the formula

25  $RC_2H_4-MgX$  by reacting in a Grignard reagent solvent a compound having the formula  $R-C=CH_2$  with a Grignard reagent having the formula  $R^1MgX$  in the presence of titanium and zirconium compounds as catalysts more specifically recited above, where R,  $R^1$ , and X have the meanings given above.

30 Our process permits the use of long-chain olefins, which have now become quite available and inexpensive, for making these Grignard reagents. Furthermore, these olefins are readily available in contrast to the unavailability of and often difficulty in preparing the halides of organic compounds of equivalent chain length for reaction with the magnesium to make usual Grignard reagents. Furthermore, by means of our process we are able to make highly desirable Grignard reagents from

45 readily available and inexpensive alkyl halides and olefins.

In the specification and claims, the following definitions will be used:

50 "Grignard solvent medium" is intended to mean those liquid media which are employed for making Grignard reagents. Included among these Grignard solvent media may be mentioned the dialkyl ethers (e.g., dimethyl ether, diethyl ether, dipropyl ether, methyl

55 ethyl ether, diisopropyl ether and ethyl butyl ether); cyclic oxygen-containing aliphatic compounds (e.g., tetrahydrofuran, and dioxane); alkyl aryl ethers (e.g., anisole and phenetole); the "Cellosolves" ("Cellosolve" is a Registered Trade Mark) (e.g., the dimethyl ether of ethylene glycol and the di-

60 butyl ether of ethylene glycol); the diethyl ether of diethylene glycol or pyridine.

"Halides of titanium" and "halides of

65 zirconium" are intended to mean not only

inorganic halides of these two metals (including oxyhalides, such as oxychlorides) but also halides of these two metals in which organic radicals are attached directly to the titanium or zirconium atoms. "Alkoxides" and "aryloxides" of titanium and zirconium are intended to include not only compounds where such organoxides are the sole group attached indirectly to the zirconium and titanium atoms, but also includes such organoxides attached to titanium and zirconium which also contain organic groups attached directly to titanium and zirconium; the terms are also intended to include polymeric as well as monomeric titanates and zirconates.

The term "monovalent organic radical" which is to be free of substituents reactive with compounds of the formula  $R^1MgX$ , is intended to mean those organic radicals which do not have any substituent which will react readily with the aforesaid Grignard reagent and preferably these substituents are substantially inert under any condition of reaction. Thus, one should avoid any organic radicals representing R which contain such substituents as the carboxy group, ketone group, nitro group, primary and secondary amino groups.

Among the radicals which R may be are, for instance, alkyl, including cycloalkyl (e.g., methyl, ethyl, propyl, isopropyl, butyl, hexyl, decyl, dodecyl, cyclopentyl and cyclohexyl); aryl radicals (e.g., phenyl, naphthyl and biphenyl); alkaryl radicals (e.g., tolyl, xylyl and ethyl phenyl); aralkyl radicals (e.g., benzyl and phenyl-ethyl); alkenyl radicals (e.g., vinyl, allyl, crotyl, cyclohexenyl and cyclopentenyl). In addition to R being the groups recited above, R can also be the same groups which are further substituted by other substituents, where one or more of the hydrogen atoms on the aforesaid groups are substituted by atoms or groups which may be aliphatic (e.g., methyl, ethyl, vinyl, propyl, propenyl, butyl, amyl, hexyl and octyl, and isomers and homologues thereof); alkoxy (e.g., methoxy, ethoxy, vinyloxy, propoxy, propen-1-oxy and butoxy, and isomers and homologues thereof); halogen and halogen-substituted radicals (e.g., chlorine, fluorine, bromine, bromotolyl, chlorobromonaphthyl, betachloro-ethyl, parachlorophenyl, tetrachlorophenyl, bromotolyl, methoxyphenyl and phenoxyphenyl, and isomers and homologues thereof); and aryloxy (e.g., phenoxy, tolyloxy, xylyloxy, chlorophenoxy and chloronaphthoxy, and isomers and homologues thereof). R may also be an organosilyl radical, e.g., trimethylsilyl, triphenylsilyl, trimethylsiloxy radicals; the pyridyl radical; organomercurio compounds, e.g., methylmercurio ( $CH_3S-$ ) and phenylmercurio ( $C_6H_5S-$ ).

Specific examples which compounds of formula  $R-C=CH_2$  may be are, for instance,

70

75

80

85

90

95

100

105

110

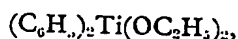
115

120

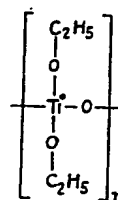
125

- propylene, 1-butene, 3-methylbutene-1, isoprene, 1-pentene, 1-hexene, 1-dodecene, 3-methyl-1-pentene, vinylcyclohexane, 4-vinylcyclohexene, allyl methyl sulfide, allyl benzene, styrene, butadiene, *m*-chlorostyrene, *p*-methylstyrene, 4-chloro-1-hexene, 2-methyl-1,5-hexadiene, allyl phenyl ether, 5,5,5-trifluoro-1-pentene, 3-vinylthiophene, 4-vinylpyridine, vinyl thioethyl ether, allyltrimethylsilane, vinyltriphenylsilane and vinylheptamethylcyclotetrasiloxane; *p*-bromostyrene, methoxystyrene (including its isomers and homologues), phenoxy styrene (including its isomers and homologues).
- 15  $R^1$  in the above formula is an alkyl radical of at least two carbon atoms, preferably from 2 to 6 carbon atoms, for instance, ethyl, propyl, isopropyl, butyl, amyl, hexyl and 2-ethyl hexyl. Among the Grignard reagents which may be used of the formula  $R^1MgX$  are, for instance, ethyl magnesium bromide, *n*-propyl magnesium bromide, *n*-propyl magnesium chloride, isopropyl magnesium chloride, 1-butyl magnesium bromide and 3-amylmagnesium bromide.

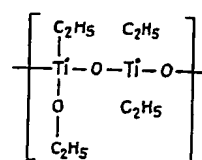
- Among the halides of titanium, halides of zirconium, alkoxides of titanium, aryloxides of titanium, alkoxides of zirconium, and aryloxides of zirconium which may be employed as the catalytic agents in the above reaction may be mentioned, for instance, titanium tetrachloride, titanium tetrabromide, titanium tetraiodide, zirconium tetrachloride, zirconium tetrafluoride, zirconium tetraiodide, zirconium oxychloride, zirconium oxybromide, ethyl titanium trichloride, monomeric titanates and monomeric zirconates of the formula  $R_mTi(OR)_{4-m}$  and  $R_mZr(OR)_{4-m}$  where R has the meaning given above (and may stand for the same or different radicals) and m is a whole number equal to from 0 to 3, inclusive. Examples of such titanates and zirconates are, for example, tetraethyltitanate, tetraethylzirconate, tetrabutyltitanate, tetrapropylzirconate, phenyl triisopropyl titanate, tetraphenyl titanate, tetraphenylzirconate, methyl titanium triethoxide having the formula  $CH_3Ti(OC_2H_5)_3$ , diphenyl titanium diisopropoxide, phenyl titanium triisopropoxide, diphenyl titanium diethoxide having the formula



- tributylethylzirconate, phenyltriethylzirconate and dicyclopentadienyl titanium dichloride. Polymers of the titanates and of the zirconates where some or all of the valencies are substituted by organoxy groups also may be used. Included among such compositions may be mentioned, for instance, polyethyltitanate having the formula



where n is a whole number greater than 1, for instance, 5 to 1000 or more, polybutyltitanate and polyethylzirconate. The presence of branched chains in the polymeric titanates and zirconates is not precluded nor is the presence of organic radicals attached directly to titanium or to zirconium by carbon-titanium or carbon-zirconium linkages, respectively. As examples of the latter compositions may be mentioned polymers having the unit



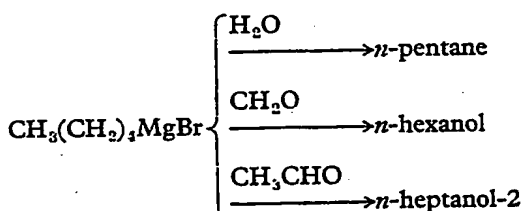
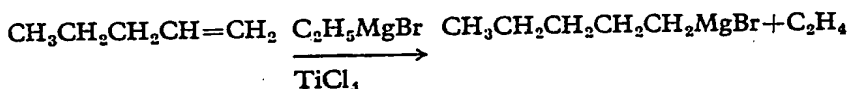
Many of the polytitanates and polyzirconates, especially those of the linear type, may be terminated by titanium- or zirconium-bonded hydroxyl groups.

The manner whereby our process is carried out is relatively simple. Having prepared the usual Grignard reagent (of the formula  $R^1MgX$ ) in the Grignard solvent, it is advantageous to add the olefin compound and cool the reaction mixture to below room temperature, for instance, from around  $-5^\circ$  to about  $15^\circ$  C. Thereafter, a small amount of the titanium or zirconium catalyst (hereinafter referred to as "catalyst") is added and the mixture of ingredients allowed to come to room temperature or heated to as high as  $200^\circ$  C. Generally, we have found that heating the mixture of ingredients at the reflux temperature of the mass (with stirring) is adequate for carrying out the reaction. Higher temperatures can be used by employing solvents whose boiling points are higher or else resorting to super-atmospheric pressure conditions. The time of heating may be varied depending upon such factors as the olefin and Grignard used and the concentration of catalyst. We have found that within 15 minutes to about 20 hours, the reaction has essentially gone to completion. Thereafter, the new Grignard reagent, still in solution in the Grignard solvent and obtained from the reaction of the

olefinic compound with the usual Grignard reagent, can then be treated with various agents designed to make the final products usually derived through the medium of the Grignard reaction.

- 5 The reaction between the usual Grignard reagent and the olefinic compound constitutes an exchange reaction whereby the olefinic compound replaces the alkyl group of the Grignard reactant. Usually the attachment to the magnesium atom is through the medium of the terminal carbon atom of the olefinic unsaturation. In some instances, this attachment may occur through the beta carbon atom of the olefinic group, especially, where one is

using aromatic-substituted olefinic compounds. Illustrative of the mechanism whereby the new Grignard reagents are prepared from the olefinic compounds are the following equations which are based on the reaction of pentene-1 with a Grignard reagent specifically, ethyl magnesium bromide, employing titanium tetrachloride as the catalyst. The following equations show not only the means of attachment through the olefinic carbon atom, but also the products which are obtainable as a result of further treating the new Grignard reagent with reactants normally employed to form materials, such as alkanes, alcohols, esters and acids.



- 35 It will be apparent to those skilled in the art that instead of employing the conditions recited above, the reaction conditions may be altered whereby the usual Grignard reagent dissolved in the Grignard solvent is mixed with the catalyst; thereafter the olefin is added, after which the reaction mixture is heated at a temperature which is suitable for converting the usual Grignard reagent to the desired Grignard derivative derived from the olefinic compound used in the reaction mixture.

- 40 The amount of catalyst used can vary widely. We may employ from as low as trace amounts of the catalyst (mixtures of catalysts can also be used), for instance, from about 0.1%, by weight, to as high as 15% or more, by weight, based on the calculated weight of the starting Grignard reagent. No particular advantage is derived from using excessive amounts of the catalyst.

- 50 The new Grignard reagents prepared in accordance with our process can be reacted in well known manners associated with Grignard reactions with the various reactants designed to give the desired product. Thus, by reacting the Grignard reagent with aldehydes (e.g., formaldehyde and acetaldehyde), one obtains alcohols. When the Grignard reagent is reacted with carbon dioxide, one obtains acids. When one adds a ketone (e.g., acetone, methyl ethyl ketone or dibutyl ketone), one obtains an alcohol. The addition of organic orthoformates (e.g., ethyl orthoformate and

propyl orthoformate) to the newly formed Grignard reagent yields acetals. The reactions between the newly formed Grignard reagent and the above other reactants to form the ultimately desired product are reactions which are well documented in the art as, for instance, in the book "Grignard Reactions of Non-metallic Substances" by M. S. Kharasch and Otto Reimuth, published by Prentice-Hall, New York, N.Y. (1954).

In order that those skilled in the art may better understand how the present invention may be practised, the following examples are given by way of illustration and not by way of limitation. All parts are by weight.

#### EXAMPLE 1

In this example, the *n*-propyl Grignard used in the succeeding examples was prepared typically as follows. A solution of about 135 parts of *n*-propyl bromide in about 71 parts diethyl ether was slowly added to 24.3 parts magnesium in 142 parts ether over a period of about 30 minutes in a reaction vessel equipped with a stirrer, dropping funnels and a reflux condenser connected to a Dry-Ice trap protected by a nitrogen by-pass. The mixture was then cooled in ice. This Grignard reagent, which had the formula



in the ether solvent, was used in many of the following examples in the reaction with the

various olefins employing the titanium or zirconium catalyst. The same or similar technique was used to make the other Grignard reagents recited below.

#### 5 EXAMPLE 2

A Grignard reagent was prepared from 0.1 mole of *n*-propyl bromide and 0.1 mole magnesium in 40 ml. of diethyl ether, was combined with 13.4 grams (0.1 mole) of *p*-methoxystyrene and the solution cooled to 0°C. Thereafter 0.4 ml. of titanium tetrachloride was added and the mixture was heated at the reflux temperature of the mass for 2 hours, cooled to 0°C. again and a second portion of 0.1 ml. of titanium tetrachloride added. After this addition, the mixture was again heated at reflux for 16 hours, and then cooled to -13°C. Dry carbon dioxide was then added at a rate sufficient to maintain the temperature at about -5°C. After one hour, the temperature dropped to -13°C., and did not rise when the flow rate was increased. The magnesium salt was decomposed by the addition of ice and 20% H<sub>2</sub>SO<sub>4</sub>. The ether layer was separated and the aqueous phase was again extracted with ether. The combined ether extracts were extracted with 25% aqueous NaOH solution and the aqueous phase separated and acidified with concentrated HCl. A liquid separated which was removed, and the aqueous phase was extracted with benzene and the benzene solution was added to the previously separated organic liquid. After drying, the mixture was distilled at atmospheric pressure to remove benzene and other volatiles. After stripping under vacuum, there remained 8.6 grams of a brown oil having a neutral equivalent of 194 and comprising *p*-methoxyhydratropic acid. The oil was refluxed with 500 ml. water and treated with decolorising carbon. On cooling the filtrate, colorless crystals melting between 54—56°C. were obtained. The residue was extracted with 500 ml. of boiling water yielding a second crop of crystals of the acid melting between 54—56°C. Recrystallisation of both mixtures of crystals from a benzene-petroleum ether mixture yielded pure *p*-methoxyhydratropic acid having a melting point of 55.5—56°C. The melting point of a mixture of this material with a sample of *p*-methoxyhydratropic acid prepared by another method was undepressed.

#### 55 EXAMPLE 3

To a Grignard reagent prepared from 0.5 mole of *n*-propyl bromide in 200 ml. of ether was added 55 grams (0.5 mole) of vinylcyclohexane. The solution was cooled to 0°C., 1.05 ml. of titanium tetrachloride was added and the mixture was heated at reflux for two hours. The mixture was then cooled to 0°C., 0.45 ml. of titanium tetrachloride was added and again the mixture refluxed for 16 hours

to yield the Grignard reagent of vinylcyclohexane. After diluting the reaction mixture with 200 ml. of ethyl ether, the mixture was cooled to -13°C. and dry carbon dioxide was added similarly as in Example 2. The magnesium salt was decomposed by the addition of ice and 20% sulfuric acid. The ether layer was separated and the aqueous phase was extracted with ether. The combined ether extracts were extracted with 25% aqueous sodium hydroxide solution and the aqueous phase was separated and acidified with concentrated hydrochloric acid. The yellow oil which separated was drawn off. The aqueous phase was extracted with 15 ml. of benzene and the benzene solution was added to the yellow oil and dried over anhydrous magnesium sulfate. Distillation yielded 38.2 grams of  $\beta$ -cyclohexylpropionic acid boiling between 114—115°C./1.5 mm.,  $n_D^{20}$  1.4647. The acid had a neutralisation equivalent of 158, compared with the theoretical value of 156.

#### EXAMPLE 4

To 0.5 mole *n*-propylmagnesium bromide in 500 ml. diethyl ether was added at 0°C., 56 grams 1-octene (0.5 mole) and 1.5 ml. titanium tetrachloride. The mixture was heated for 24 hours at the reflux temperature of the mass to give the Grignard reagent derived from 1-octene. A 25 ml. sample was hydrolysed with 15 grams of ice and 5 ml. of hydrochloric acid to give a 58.2% yield of octane.

#### EXAMPLE 5

A solution of 0.175 mole *n*-propylmagnesium bromide, 0.25 ml. titanium tetrachloride and 9.8 grams 1-octene was refluxed for 30 hours to form the Grignard derived from 1-octene. The mixture of ingredients was cooled to 0°C. and 0.25 mole triethylorthoformate was added. The mixture was then heated at the reflux temperature of the mass for 60 hours, the diethyl ether was decanted and the remaining solid material was washed twice with 50 ml. of ethyl ether. Distillation of the ether solution yielded 7.3 grams of pelargonic diethyl acetal having a boiling point of 64—66°C. at 25 mm. and having  $n_D^{20}$  1.4219.

#### EXAMPLE 6

In this example, to a Grignard reagent prepared from 0.5 mole *n*-propyl bromide in 200 ml. of diethyl ether, was added 42 grams (0.5 mole) 1-hexene. The solution was cooled to 0°C., 1.05 ml. of titanium tetrachloride was added, and the mixture was heated under reflux for two hours. The mixture was again cooled at 0°C., 0.45 ml. titanium tetrachloride was added, and refluxing was continued for 16 hours. At the end of this time the newly formed Grignard reaction product from the 1-hexene was mixed with 73.5 grams (0.75 mole) cyclohexanone added at

about 0° C. and the mixture was stirred for one hour at room temperature; the magnesium salt was decomposed by the addition of ammonium chloride and the ether layer was distilled, yielding 21.45 grams of 1-hexylcyclohexanol having a boiling point of 114—116° C./4 mm.,  $n_D^{20}$  1.4665.

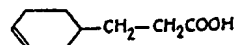
#### EXAMPLE 7

To 0.5 mole of *n*-propylmagnesium bromide in 400 ml. of ether was added 56 grams (0.5 mole) 1-octene and 1.5 ml. titanium tetrachloride at a temperature of about 0° C. This mixture was stirred and heated at reflux temperature for 18 hours to give the Grignard reagent derived from the 1-octene. The reaction mixture was cooled and a stream of dry carbon dioxide was passed over the surface of the mixture at such a rate that the temperature stayed below -5° C. When the reaction was complete to form pelargonic acid, the temperature of the system was lowered to -20° C. and 300 ml. of methanol for esterification purposes was added at such a rate as to keep the temperature between -20° and -30° C. After the methanol had been added, dry hydrogen chloride was led into the reaction vessel, the reaction mixture stirred for 2½ hours, poured into 600 grams ice, the ether phase separated and the aqueous layer extracted with ether. After drying, the organic material was distilled to give 34.3 grams methyl pelargonate boiling at 97—99° C./12 mm.,  $n_D^{20}$  1.4205.

#### EXAMPLE 8

To 1.0 mole of *n*-propylmagnesium bromide in 800 ml. of diethyl ether cooled to 0° C. was added 108 grams (1 mole) of 4-vinylcyclohexene and 3.2 ml. of titanium tetrachloride. The mixture was heated at the reflux temperature of the mass for 18 hours to form the Grignard reagent of cyclohexene, and thereafter cooled to -10° C. Dry carbon dioxide was passed over the surface of the reaction mixture at such a rate that the temperatures stayed below -5° C. When increasing the flow of carbon dioxide no longer raised the temperature, the carbon dioxide addition was stopped. At this point 1.0 liter of 25% (by volume) aqueous sulfuric acid was added. After stirring for 30 minutes, the ether phase was separated and the aqueous layer extracted twice with 75 ml. portions of ether. The ether layers were combined and extracted three times with a total of 350 ml. of 25% sodium hydroxide. At each extraction, enough water was added to dissolve the soap that formed. The aqueous basic extract was heated to boiling and enough distillate was removed to reduce the volume by 10%. The liquid was then cooled and concentrated hydrochloric acid added until the aqueous phase was acid to congo red. The organic layer was then separated and the water layer

extracted with 50 ml. portions of chloroform. All the organic material was combined and dried over anhydrous magnesium sulfate. After removing the chloroform by distillation, the residue was fractionated to give a total of 44 grams of  $\beta$ -( $\Delta^2$ -cyclohexenyl) propionic acid having the formula



boiling point 99—102° C./0.2 mm.; melting point 31—2° C.  $n_D^{20}$  1.4732. Analysis of this compound showed that it contained 69.8% carbon and 9.3% hydrogen as contrasted to the theoretical values of 70.1% carbon and 9.2% hydrogen.

#### EXAMPLE 9

A Grignard reagent was prepared from 0.5 mole *n*-propyl bromide in 200 ml. diethyl ether; 45 grams 1-pentene (or *n*-pentene) was added and the solution was cooled to 0° C. After addition of 3.9 grams of isopropyl tetra-titanate [(C<sub>3</sub>H<sub>7</sub>O)<sub>4</sub>Ti] the mixture was heated at the reflux temperature of the mass for 16 hours to form the Grignard reagent of 1-pentene. Thereafter, 200 ml. of ethyl ether was added and the mixture was treated with 20 grams formaldehyde and the product isolated by decomposing the mixture by the addition of ice and 20% aqueous sulfuric acid. After steam distillation, the organic layer was separated and distilled yielding 11.8 grams of 1-hexanol having a boiling point of 87° C./49 mm.,  $n_D^{20}$  1.4182.

The following example shows the effect of omitting the catalyst from the reaction described in Example 9 of the olefinic compound with the Grignard reagent.

#### EXAMPLE 10

A Grignard reagent prepared from 0.5 mole of *n*-propyl bromide and 0.55 mole of magnesium in 200 ml. of ether was heated under reflux for 18 hours with 45 grams of 1-pentene. Formaldehyde was added to the mixture and the mixture was decomposed with ice and sulfuric acid and distilled with steam similarly as was done in Example 9. The organic phase of the distillate was separated, dried, and distilled yielding *n*-butyl alcohol. No *n*-hexanol could be detected on analysis of the crude product and of the distillation residue.

#### EXAMPLE 11

A Grignard reagent was prepared from 0.5 mole *n*-propyl bromide in 400 ml. of diethyl ether. About 45 grams 1-pentene was added to the Grignard reagent and the solution was cooled to 0° C. After addition of 3.34 grams of dicyclopentadienyltitanium dichloride, the



mixture was heated at the reflux temperature of the mass for 12 hours (to give a new Grignard reagent derived from the 1-pentene), and then reacted with formaldehyde and the reaction product isolated as in Example 9. Fractional distillation yielded 10.2 grams 1-hexanol having a boiling point 90°C./50 mm.,  $n_D^{20}$  1.4182.

#### EXAMPLE 12

A Grignard reagent was prepared from 0.5 mole n-propyl bromide in 200 ml. of diethyl ether. 45 grams of 1-pentene was added, and the solution was cooled to 0°C. At this point 3.3 grams of zirconium tetrachloride was added and the mixture was heated at the reflux temperature of the mass for 16 hours to give the Grignard derivative of 1-pentene. Thereafter 200 ml. of diethyl ether was added to the mixture, the latter cooled to 0°C. and about 20 grams formaldehyde was introduced in a slow stream of nitrogen. The mixture was decomposed by the addition of ice and 20% aqueous sulfuric acid. After steam distillation, the organic layer was separated and distilled, yielding 14.4 grams of 1-hexanol having a boiling point 85°C./45 mm.,  $n_D^{20}$  1.4186.

#### EXAMPLE 13

To a Grignard reagent prepared from 0.1 mole magnesium and 0.1 mole isopropyl bromide in 50 ml. of diethyl ether was added at 0°C.  $2.2 \times 10^{-3}$  moles of titanium tetrachloride and 0.1 mole of 1-pentene. The reaction mixture was heated at the reflux temperature of the mass for 18 hours to form a new Grignard reagent derived from 1-pentene having the formula  $\text{CH}_3(\text{CH}_2)_4\text{—MgBr}$ . The reaction mixture was then hydrolysed with 5 grams of ammonium chloride in 15 ml. of water. After the solid residue from the reaction had been washed with 25 ml. of diethyl ether, the product was dried over magnesium sulphate. Analysis of this material showed that a good yield of n-pentane had been obtained. When the reaction described above was carried out with the exception that n-propyl bromide was used to make the initial Grignard reagent in place of the isopropyl bromide, similar results were obtained with the exception that a somewhat larger yield of n-pentane was realised.

#### EXAMPLE 14

To a Grignard reagent prepared from 0.5 mole of n-propyl bromide in 200 ml. of diethyl ether was added 42 grams (0.5 mole) of 4-methyl-1-pentene. The solution was cooled to 0°C., 1.05 ml. titanium tetrachloride was added, and the mixture was heated at the reflux temperature of the mass for 2 hours and cooled again to 0°C. A second portion of 0.35 ml. of titanium tetrachloride was added, the mixture was refluxed for 16 more hours to yield the new Grignard reagent derived from the aforesaid

pentene. The reaction mixture was then again cooled to 0°C. and a solution of 28 ml. acetaldehyde in 50 ml. diethyl ether was added over a period of 1 hour. Since the mixture still showed evidence that some Grignard reagent was present and unreacted, a solution of 5 ml. acetaldehyde in 25 ml. of diethyl ether was added and the mixture was again stirred at room temperature (about 22°C.) for ten minutes. Thereafter, the reaction mixture was decomposed by the addition of ammonium chloride solution. The ether layer was separated and distilled, yielding 24.2 grams of 6-methyl-2-heptanol, boiling point 82–85°C./22 mm.,  $n_D^{20}$  1.4248.

#### EXAMPLE 15

A Grignard reagent was prepared from 0.5 mole of n-propyl bromide and 0.55 mole magnesium in 200 ml. of diethyl ether. To this Grignard reagent was added 59 grams (0.5 mole) of allyl benzene. The solution was cooled to 0°C. and 1 ml. of titanium tetrachloride was added. The mixture was heated at the reflux temperature of the mass for 16 hours to form the new Grignard reagent derived from the allyl benzene. The reaction mixture was cooled, and treated with dry carbon dioxide as shown in previous examples. The mixture was decomposed with 25% aqueous sulfuric acid and extracted with diethyl ether. The ether solution was in turn extracted with 25% aqueous sodium hydroxide solution. After boiling for a short time to remove volatile organic compounds, the sodium hydroxide solution was cooled and acidified with 36% hydrochloric acid. The mixture was extracted with diethyl ether and the ether was evaporated at 50°C. On cooling, 50.9 grams of waxy plates of gamma-phenylbutyric acid were obtained. Recrystallisation of the waxy plates from water yielded the pure acid having a melting point of 50.5–51°C. The neutralisation equivalent was 166, compared to the theoretical value of 164.

#### EXAMPLE 16

To 1.0 mole of n-propylmagnesium bromide in 800 ml. of ethyl ether were added 108 grams (1.0 mole) of 4-vinylcyclohexene and 3.0 ml. of titanium tetrachloride at 0°C. The reaction mixture was refluxed for 16 hours then cooled to 0°C. and a stream of dry air passed over the surface of the stirred mixture for 1 hour. The air was then replaced by oxygen for an additional 1.5 hours. At the end of this time the reaction mixture was poured into 800 ml. of water containing 100 ml. of hydrochloric acid. The aqueous phase was extracted with a total of 600 ml. of ethyl ether. After drying over magnesium sulfate the product was distilled. A yield of 50 grams of  $\beta$ -( $\Delta^2$ -cyclohexenyl) ethanol (b.p. 92–94°C./4 mm.,  $n_D^{20}$  1.4835) was obtained.

## EXAMPLE 17

A solution of 0.5 mole of *n*-amylmagnesium bromide in 400 ml. of ethyl ether was cooled to 0° C. and 56 grams of 1-octene was added, followed by 1.5 ml. of titanium tetrachloride. After refluxing for 16 hours, the mixture was cooled to 0° C., and 29 grams of acetone was added over a period of 20 minutes. The reaction was then stirred for 2 hours at room temperature. After hydrolysis with 30 ml. of water and 55 grams of ammonium chloride, the ether was decanted off and the residue washed with an additional 200 ml. of ether. Distillation yielded the alcohol, 2-methyl-decanol-2 (b.p. 82—3° C./1 mm.,  $n_D^{20}$  1.4380).

## EXAMPLE 18

52 grams (0.5 mole) of styrene was added to a Grignard reagent prepared from 0.5 mole of *n*-propyl bromide and 0.55 mole of magnesium in 100 ml. of diethyl ether. The solution was cooled to 0° C., 1.05 ml. of titanium tetrachloride was added and the mixture was then stirred and heated at reflux temperature of the mixture for 2 hours. The mixture was then cooled, 0.45 ml. of titanium tetrachloride was added, and refluxing was continued for 16 hours. The mixture was then diluted with 200 ml. of diethyl ether, cooled to -13° C., and treated with carbon dioxide as in previous examples. The mixture was decomposed with sulfuric acid and the organic layer was separated. The aqueous phase was extracted with diethyl ether and the ether extract combined with the organic layer previously obtained. The ether solution was extracted with 25% aqueous sodium hydroxide solution. The sodium hydroxide solution was heated to remove volatile organic compounds and then cooled and acidified with concentrated hydrochloric acid. The mixture was extracted with diethyl ether and the ether extract was distilled yielding 37.6 grams of hydratropic acid boiling at 125° C. at 3 mm. pressure and having a refractive index  $n_D^{20}$  1.5230.

It will of course be apparent to those skilled in the art that in addition to the olefinic compounds employed in the foregoing examples other olefinic compounds may be used, many examples which are given above, without departing from the scope of the invention. Alternatively, the Grignard reagent with which the olefinic compounds react may also be varied widely and there is no restriction as to the type of usual Grignard reagents which may be used within the framework of the formula  $R^1MgX$ .

The conditions of reaction may be altered to fit the occasion and the concentration of the catalyst may also be modified depending upon the conditions of the reaction. It will also be apparent that the proportion of the olefinic compound to the Grignard reagent can be varied widely. It is desirable that the olefinic compound and the Grignard reactant

be present in essentially equimolar concentrations. An excess of one reactant (e.g., from a 1 to 10 molar excess) over the other is of course not precluded. Good results generally are obtained when there is present from about 0.5 to 2 moles of the olefinic compound for each mole of the starting Grignard reactant.

The Grignard reagents prepared in accordance with our process can be reacted with other reactants under conditions which usual Grignard reagents undergo, to form, for instance, alcohols, acids, esters and acetals, which in turn can be used further to form other useful compounds. Thus, the acid can be reacted with alcohols some examples of which have been given above to form esters which are useful as plasticisers for various resins, particularly vinyl halide resins, such as polyvinyl chloride. Still other compounds obtainable as a result of practising our process can be used for insect repellants or can be employed to make soaps, particularly those derived from long-chained olefinic compounds.

## WHAT WE CLAIM IS:—

1. A process of preparing a Grignard reagent having the formula  $R-C_2H_5-MgX$ , which comprises reacting in a Grignard solvent medium an olefinic hydrocarbon having the formula  $R-CH=CH_2$  with an alkyl Grignard reagent having the formula  $R^1-MgX$  in the presence of a halide of titanium or zirconium, an alkoxide of titanium or zirconium, or an aryloxide of titanium or zirconium as a catalyst, where R is a monovalent organic radical free of substituents reactive with said alkyl Grignard reagent,  $R^1$  is an alkyl radical having at least 2 carbon atoms and having at least one hydrogen on the beta carbon atom, and X is a halogen.
2. A process according to Claim 1, in which the catalyst is titanium tetrachloride.
3. A process according to Claim 1, in which the catalyst is zirconium tetrachloride.
4. A process according to Claim 1, in which the catalyst is tetra-isopropyl titanate.
5. A process according to Claim 1, in which the catalyst is dicyclopentadienyl titanium dichloride.
6. A process according to any of Claims 1 to 5, in which the olefinic hydrocarbon is styrene.
7. A process according to Claim 2, in which styrene is reacted with *n*-propyl magnesium bromide to produce phenyl-ethyl magnesium bromide.
8. A process according to any of Claims 1 to 5, in which the olefinic hydrocarbon is a vinyl cyclohexene.
9. A process according to Claim 2, in which 4-vinyl cyclohexene is reacted with *n*-propyl magnesium bromide to produce cyclohexenyl-ethyl magnesium bromide.
10. A process according to any of Claims 1 to 5, in which the olefinic hydrocarbon is 1-pentene.

11. A process according to Claim 3, in which 1-pentene is reacted with *n*-propyl magnesium bromide to produce pentyl magnesium bromide.
- 5 12. A process according to Claim 4, in which 1-pentene is reacted with *n*-propyl magnesium bromide to produce pentyl magnesium bromide.
- 10 13. A process according to Claim 5, in which 1-pentene is reacted with *n*-propyl magnesium bromide to produce pentyl magnesium bromide.
- 15 14. A process according to any of Claims 1 to 5, in which the olefinic hydrocarbon is vinyl cyclohexane.
- 15 15. A process according to any of Claims 1 to 5, in which the olefinic hydrocarbon is a methoxy styrene, especially *p*-methoxy styrene.
- 20 16. A process of preparing a Grignard reagent having the formula  $R-C_2H_4-MgX$  substantially as hereinbefore described with reference to and as illustrated by any of Examples 2 to 9 and 11 to 18.
- 25 17. A Grignard reagent having the formula  $R-C_2H_4-MgX$  whenever prepared by the process according to any of Claims 1 to 16.
- 30 18. A method of forming a compound such as an acetal, an acid, an alcohol, or an alkane containing the  $R-C_2H_4$  radical, which comprises reacting a Grignard reagent according to Claim 17 under Grignard reaction conditions in well-known manner with respectively an orthoformate, carbon dioxide, an aldehyde or a ketone or oxygen, or water.
19. A method of forming hydratropic acid, which comprises reacting phenyl-ethyl magnesium bromide produced by the process according to Claim 7 with carbon dioxide. 35
20. A method of forming  $\beta$ -( $\Delta^3$ -cyclohexenyl) propionic acid, which comprises reacting the cyclohexenyl-ethyl magnesium bromide produced by the process according to Claim 9 with carbon dioxide. 40
21. A method of forming 1-hexanol, which comprises reacting the pentyl magnesium bromide produced by the process according to any of Claims 11 to 13 with formaldehyde. 45
22. A method of forming a compound such as an acetal, an acid, an alcohol, or an alkane containing the  $R-C_2H_4$  radical substantially as hereinbefore described with reference to and as illustrated by any of Examples 2 to 9 and 11 to 18. 50
23. A compound such as an acetal, an acid, an alcohol, or an alkane containing the  $R-C_2H_4$  radical whenever formed by the method according to any of Claims 18 to 22. 55

THIEMANN, SON & CO.,

Chartered Patent Agents,  
Prestige House, 14 to 18, Holborn,  
London, E.C.1.  
Agents for the Applicants.

Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press (Leamington) Ltd.—1964. Published by The Patent Office, 25 Southampton Buildings, London, W.C.2, from which copies may be obtained.

